ClinicalEvidence

Sore throat

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ABSTRACT

INTRODUCTION: About 10% of people present to primary healthcare services with sore throat each year. The causative organisms of sore throat may be bacteria (most commonly Streptococcus) or viruses (typically rhinovirus), although it is difficult to distinguish bacterial from viral infections clinically. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical questions: What are the effects of interventions to reduce symptoms of acute infective sore throat? What are the effects of interventions to prevent complications of acute infective sore throat? We searched: Medline, Embase, The Cochrane Library, and other important databases up to January 2010 (Clinical Evidence reviews are updated periodically, please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). RESULTS: We found 8 systematic reviews, RCTs, or observational studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. CONCLUSIONS: In this systematic review we present information relating to the effectiveness and safety of the following interventions: antibiotics, corticosteroids, non-steroidal anti-inflammatory drugs, paracetamol, and probiotics.

QUESTIONS

INTERVENTIONS

TREATING SYMPTOMS

Likely to be beneficial

Trade off between benefits and harms

Unknown effectiveness

PREVENTING COMPLICATIONS

Trade off between benefits and harms

Covered elsewhere in Clinical Evidence

Acute bronchitis

Acute otitis media

Acute sinusitis

Common cold

Tonsillitis

Key points

- Sore throat is an acute upper respiratory tract infection that affects the respiratory mucosa of the throat.
- About 10% of people present to primary healthcare services with sore throat each year.

  The causative organisms of sore throat may be bacteria (most commonly *Streptococcus*) or viruses (typically rhinovirus), but it is difficult to distinguish bacterial from viral infections clinically.
- NSAIDs may reduce the pain of sore throat at 24 hours or less, and at 2 to 5 days.

  NSAIDs are associated with gastrointestinal and renal adverse effects.
- Paracetamol seems to effectively reduce the pain of acute infective sore throat after a single dose, or regular doses over 2 days.
- Antibiotics can reduce the proportion of people with symptoms associated with sore throat at 3 days.

  Reduction in symptoms seems greater for people with positive throat swabs for *Streptococcus* than for people with negative swabs.

  Antibiotics are generally associated with adverse effects such as nausea, rash, vaginitis, and headache, and widespread use may lead to bacterial resistance.
- Antibiotics may also reduce suppurative and non-suppurative complications of group A beta-haemolytic streptococcal pharyngitis, although non-suppurative complications are rare in industrialised countries.
- Corticosteroids added to antibiotics may reduce the severity of pain from sore throat in adults compared with antibiotics alone. Effects in children are uncertain.

  Most trials used a single dose of corticosteroid.

  However, data from other disorders suggest that long-term use of corticosteroids is associated with serious adverse effects.

- Super-colonisation with *Streptococcus* isolated from healthy individuals apparently resistant to infections from *Streptococcus* may reduce recurrence of sore throat, although there is currently no evidence to suggest it may treat symptoms of acute sore throat.

DEFINITION

Sore throat is an acute upper respiratory tract infection that affects the respiratory mucosa of the throat. Since infections can affect any part of the mucosa, it is often arbitrary whether an acute upper respiratory tract infection is called "sore throat" ("pharyngitis" or "tonsillitis"), "common cold", "sinusitis", "otitis media", or "bronchitis" (see figure 1, p 13). Sometimes, all areas are affected (simultaneously or at different times) in one illness. In this review, we aim to cover people whose principal presenting symptom is sore throat. This may be associated with headache, fever, and general malaise. Suppurative complications include acute otitis media (most commonly), acute sinusitis, and peritonsillar abscess (quinsy). Non-suppurative complications include acute rheumatic fever and acute glomerulonephritis.This review does not include people with previous rheumatic fever or previous glomerulonephritis, who are importantly different from the general population of people with sore throats. It also does not include people who are clinically seriously unwell (as these people are typically not included in the primary studies).

INCIDENCE/ PREVALENCE

There is little seasonal fluctuation in sore throat. About 10% of the Australian population present to primary healthcare services annually with an upper respiratory tract infection consisting predominantly of sore throat. [1] This reflects about one fifth of the overall annual incidence. [1] However, it is difficult to distinguish between the different types of upper respiratory tract infection. [2] A Scottish mail survey found that 31% of adult respondents reported a severe sore throat in the previous year, for which 38% of these people visited a doctor. [3]

AETIOLOGY/ RISK FACTORS

The causative organisms of sore throat may be bacteria (*Streptococcus*, most commonly group A beta-haemolytic, but sometimes *Haemophilus influenzae*, *Moraxella catarrhalis*, and others) or viruses (typically rhinovirus, but also coronavirus, respiratory syncytial virus, metapneumovirus, Epstein–Barr virus, and others). It is difficult to distinguish bacterial from viral infections clinically. Features thought to indicate *Streptococcus* infection are: fever >38.5 °C, exudate on the tonsils, anterior neck lymphadenopathy, and absence of cough. [4] Sore throat can be caused by processes other than primary infections, including GORD, physical or chemical irritation (e.g., from nasogastric tubes or smoke), and occasionally hay fever. However, we consider only primary infections in this review.

PROGNOSIS

The untreated symptoms of sore throat disappear by 3 days in about 40% of people, and untreated fevers in about 85%. [5] By 1 week, 85% of people are symptom free. This natural history is similar in *Streptococcus*-positive, *Streptococcus*-negative, and untested people.

AIMS OF INTERVENTION

To relieve symptoms and to prevent suppurative and non-suppurative complications of sore throat.

OUTCOMES

Symptom severity: reduction in severity and duration of symptoms (sore throat pain, general malaise, headache, and fever); **prevention of complications:** reduction in suppurative complications (acute otitis media, acute sinusitis, and quinsy) and non-suppurative complications (acute rheumatic fever and acute glomerulonephritis); **recurrence:** recurrence of symptoms, time off work or school; patient satisfaction; healthcare utilisation; **adverse effects** of treatment.

METHODS

Clinical Evidence search and appraisal January 2010. The following databases were used to identify studies for this systematic review: Medline 1966 to January 2010, Embase 1980 to January 2010, and The Cochrane Database of Systematic Reviews 2009, Issue 4 (1966 to date of issue). An additional search within The Cochrane Library was carried out for the Database of Abstracts of Reviews of Effects (DARE) and the Health Technology Assessment (HTA) database. We also searched for retractions of studies included in the review. Abstracts of the studies retrieved from the initial search were assessed by an information specialist. Selected studies were then sent to the contributor for additional assessment, using predetermined criteria to identify relevant studies. Study design criteria for inclusion in this review were: published systematic reviews of RCTs and RCTs in any language. RCTs had to contain 20 or more individuals, of whom 80% or more were followed up. Open trials were included if the outcomes were objective (otherwise all studies described as "open", "open label", or "non-blinded" were excluded). There was no minimum length of follow-up required to include studies. We included systematic reviews of RCTs and RCTs where harms of an included intervention were studied applying the same study design criteria for inclusion as we did for benefits. In addition we use a regular surveillance protocol to capture harms alerts from organisations such as the FDA and the MHRA, which are added to the reviews as required. We excluded RCTs that only provided data about bacteriological studies of the throat, because bacteriological cure is not a clinically useful outcome for spontaneously remitting illness. To aid readabil-

ity of the numerical data in our reviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 15). The categorisation of the quality of the evidence (high, moderate, low, or very low) reflects the quality of evidence available for our chosen outcomes in our defined populations of interest. These categorisations are not necessarily a reflection of the overall methodological quality of any individual study, because the Clinical Evidence population and outcome of choice may represent only a small subset of the total outcomes reported, and population included, in any individual trial. For further details of how we perform the GRADE evaluation and the scoring system we use, please see our website (www.clinicalevidence.com).

QUESTION **What are the effects of interventions to reduce symptoms of acute infective sore throat?**

OPTION **ANALGESICS TO REDUCE SYMPTOMS OF ACUTE INFECTIVE SORE THROAT**

- For GRADE evaluation of interventions for Sore throat, see table, p 15 .
- Paracetamol seems to effectively reduce the pain of acute infective sore throat after a single dose, or regular doses over 2 days.
- We found no direct information from RCTs about other analgesics in the treatment of people with sore throat.
- The FDA issued a drug safety alert on the risk of rare but serious skin reactions with paracetamol (acetaminophen) (August 2013).

Benefits and harms

Analgesics versus placebo:

We found one systematic review (search date 1999, 3 RCTs, 312 people with acute moderate to severe sore throat for up to 4 days), [6] and one subsequent RCT [7] comparing paracetamol (acetaminophen) versus placebo. We found no systematic review or RCTs of other analgesics in people with sore throat.

Symptom severity

Compared with placebo Paracetamol seems more effective at reducing sore throat pain (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Symptom severity					
[6] Systematic review	81 adults, 77 children 2 RCTs in this analysis	**Mean sore throat pain score , 2 to 3 hours** with single dose of paracetamol with placebo Absolute results not reported	50% greater reduction with paracetamol than with placebo in 1 RCT; P <0.01 31% greater reduction with paracetamol than with placebo in the other RCT; P <0.05	○○○	single dose of paracetamol
[6] Systematic review	154 children Data from 1 RCT	**Sore throat pain , 2 days** with paracetamol 3 times daily with placebo Absolute results not reported	34% greater reduction with paracetamol than with placebo P <0.01	○○○	paracetamol 3 times daily
[7] RCT	241 adults with throat pain score of 7 or more measured on a 0 to 10 scale	**Pain reduction , 15 minutes** with single dose of paracetamol with placebo Absolute results reported graphically Pain reduction was measured on an 8-point scale (where 0 = no relief to 7 = complete relief)	P <0.03	○○○	single dose of paracetamol
[7] RCT	241 adults with throat pain score of 7 or more mea-	**Total pain relief scores , 6 hours**	P <0.05	○○○	single dose of paracetamol

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
	sured on a 0 to 10 scale	793 with single dose of paracetamol 631 with placebo Pain reduction was measured on an 8-point scale (where 0 = no relief to 7 = complete relief)			

Recurrence

No data from the following reference on this outcome. [6] [7]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[7] RCT	241 adults with throat pain score of 7 or more measured on a 0 to 10 scale	**Adverse effects** with single dose of paracetamol with placebo Absolute results not reported	The RCT stated that there were no serious adverse effects reported, and that no adverse effects were assessed as being related to study treatment		

No data from the following reference on this outcome. [6]

Further information on studies

Comment: None.

OPTION NSAIDS TO REDUCE SYMPTOMS OF ACUTE INFECTIVE SORE THROAT

- For GRADE evaluation of interventions for Sore throat, see table, p 15 .
- NSAIDs may reduce the pain of sore throat at 24 hours or less, and at 2 to 5 days.
- NSAIDs are associated with gastrointestinal and renal adverse effects.

Benefits and harms

NSAIDs versus placebo:

We found one systematic review (search date 1999, 12 RCTs, 1189 people with acute sore throat for up to 5 days, severity unclear) comparing NSAIDs versus placebo. [6] The review did not perform a meta-analysis. Seven RCTs (492 people) identified by the review assessed the effects of NSAIDs (including 1 RCT of oral aspirin and 1 RCT of aspirin gum) over 24 hours or less. Six RCTs (697 people) identified by the review assessed the effects of NSAIDs over >24 hours.

Symptom severity

Compared with placebo NSAIDs seem more effective at reducing sore throat symptoms at 24 hours to 5 days (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Symptom severity					
[6] Systematic review	1189 people 12 RCTs in this analysis	**Throat pain , <24 hours** with NSAIDs with placebo Absolute results not reported	All the RCTs found that NSAIDs significantly reduced throat pain compared with placebo The range of significant improvements in throat pain compared with placebo ranged from 25% to 75% P <0.05 in all RCTs	○○○	NSAIDs
[6] Systematic review	697 people 6 RCTs in this analysis	**Symptom severity, primarily throat pain , 2 to 5 days** with NSAIDs with placebo Absolute results not reported Pain was assessed using a variety of visual analogue and scoring systems	All the RCTs found that NSAIDs significantly reduced symptoms (primarily throat pain) compared with placebo The range of significant improvements in symptoms compared with placebo ranged from 33% to 93% P <0.05 in all RCTs	○○○	NSAIDs

Recurrence

No data from the following reference on this outcome. [6]

Adverse effects

No data from the following reference on this outcome. [6]

Further information on studies

[6] The review gave no information on adverse effects. However, data from systematic reviews in people with other disorders suggest that NSAIDs are associated with gastrointestinal and renal adverse effects (see review on NSAIDs).

Comment: **Clinical guide:**
NSAIDs seem effective, but have potential for adverse effects. Aspirin is best avoided in children <15 years of age owing to the rare risk of Reye's syndrome.

OPTION ANTIBIOTICS TO REDUCE SYMPTOMS OF ACUTE INFECTIVE SORE THROAT

- For GRADE evaluation of interventions for Sore throat, see table, p 15 .
- Antibiotics can reduce the proportion of people with symptoms associated with sore throat at 3 days.
- Reduction in symptoms seems greater for people with positive throat swabs for *Streptococcus* than for people with negative swabs.

- Antibiotics are generally associated with adverse effects such as nausea, rash, vaginitis, and headache, and widespread use may lead to bacterial resistance.

Benefits and harms

Antibiotics versus placebo:

We found one systematic review (search date 2008, 27 randomised or quasi-randomised trials, 12,835 people with sore throat, severity unclear) comparing antibiotics versus placebo. [5]

Symptom severity

Compared with placebo Antibiotics are more effective at reducing sore throat and headache at 3 days, particularly in people with positive throat swabs for Streptococcus (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Symptom severity					
[5] Systematic review	3621 people 15 RCTs in this analysis	**Sore throat , 3 days** 1006/2066 (49%) with antibiotics 1031/1555 (66%) with placebo	RR 0.68 95% CI 0.59 to 0.79	●○○	antibiotics
[5] Systematic review	2974 people 13 RCTs in this analysis	**Sore throat , 6 to 8 days** 246/1839 (13%) with antibiotics 206/1135 (18%) with placebo	RR 0.49 95% CI 0.32 to 0.76 The review estimated that this represents an average shortening of symptoms of sore throat by about 16 hours for the first week	●●○	antibiotics
[5] Systematic review	1334 people 7 RCTs in this analysis	**Fever , 3 days** with antibiotics with placebo Absolute results not reported	RR 0.71 95% CI 0.45 to 1.10	⟷	Not significant
[5] Systematic review	911 people 3 RCTs in this analysis	**Headache , 3 days** 122/552 (22%) with antibiotics 147/359 (41%) with placebo	RR 0.47 95% CI 0.38 to 0.58	●●○	antibiotics

Recurrence

No data from the following reference on this outcome. [5]

Adverse effects

No data from the following reference on this outcome. [5]

Further information on studies

[5] Severely unwell people were not included in the RCTs included in the systematic review. Consequently, these findings may not apply to those people.

[5] The review found limited evidence from indirect comparisons that, in people with throat swabs positive for *Streptococcus*, the absolute and relative reduction in the proportion of people with sore throat symptoms at 3

days was greater than in people with negative swabs (positive swabs: 11 trials, 471/1073 [44%] with antibiotics *v* 544/766 [71%] with placebo, RR 0.58, 95% CI 0.48 to 0.71; negative swabs: 6 trials, 262/458 [57%] with antibiotics *v* 202/278 [73%] with placebo, RR 0.78, 95% CI 0.63 to 0.97).

[5] The review gave no information about the adverse effects associated with antibiotic use. [5] However, data from systematic reviews in people with other disorders suggested that antibiotics were associated with nausea, vomiting, headache, skin rash, and vaginitis (see reviews on acute bronchitis and acute otitis media in children).

[5] The review also assessed the effects of antibiotics on streptococcal complications (see antibiotics to prevent complications of acute infective sore throat, p 11). We found no systematic review or RCTs that assessed severity of sore throat symptoms.

Comment: **Clinical guide:**
Widespread antibiotic use may lead to bacterial resistance to antibiotics (see review on acute bronchitis).

OPTION CORTICOSTEROIDS TO REDUCE SYMPTOMS OF ACUTE INFECTIVE SORE THROAT

- For GRADE evaluation of interventions for Sore throat, see table, p 15 .
- Corticosteroids added to antibiotics may reduce the severity of pain from sore throat in adults compared with antibiotics alone. Effects in children are uncertain.
- Most trials used a single dose. However, data from use of corticosteroids in other disorders suggest that long-term use of corticosteroids is associated with serious adverse effects.

Benefits and harms

Corticosteroids versus placebo in people receiving antibiotics:

We found one systematic review (search date 2008, 8 RCTs, 743 people [369 children, 374 adults], of whom 47% had exudative sore throat and 44% were positive for group A beta-haemolytic streptococcus) comparing corticosteroids versus placebo. [8] In 5 RCTs, all participants also received antibiotics; in three RCTs participants either received antibiotics if direct antigen testing or culture for *Streptococcus* was positive, or stopped antibiotics if the test was negative. The corticosteroids used were dexamethasone orally or intramuscularly (up to 10 mg, single dose, 6 RCTs), betamethasone intramuscularly (8 mg, single dose, 1 RCT), or prednisone orally (up to 60 mg, 1–2 days, 1 RCT). Two RCTs included only children, three included only adults, and three included both.

Symptom severity

Compared with placebo in people receiving antibiotics Dexamethasone, betamethasone, or prednisone (single dose or for 1–2 days), with concurrent antibiotic, are more effective than placebo at reducing time to initial pain relief, and duration of throat pain in adults with severe and exudative sore throat without evidence of group A beta-haemolytic streptococcal infection, but effects in children are unclear (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Symptom severity					
[8] Systematic review	286 adults and children 4 RCTs in this analysis	**Complete resolution of pain , 24 hours** 54/139 (39%) with oral or intramuscular corticosteroids 18/147 (12%) with placebo	RR 3.2 95% CI 2.0 to 5.1 NNT 4 95% CI 3 to 6	●●○	corticosteroids
[8] Systematic review	209 adults and children 3 RCTs in this analysis	**Complete resolution of pain , 48 hours** 74/98 (75%) with oral or intramuscular corticosteroids 52/111 (47%) with placebo	RR 1.7 95% CI 1.3 to 2.1 NNT 3 95% CI 2 to 6	●○○	corticosteroids
[8] Systematic review	Number of adults not reported 3 RCTs in this analysis	**Complete resolution of pain , 24 hours** with oral or intramuscular corticosteroids	RR 4.3 95% CI 2.3 to 8.1	●●○	corticosteroids

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
	Subgroup analysis	with placebo Absolute results not reported			
[8] Systematic review	Number of adults not reported 3 RCTs in this analysis Subgroup analysis	**Complete resolution of pain , 48 hours** with oral or intramuscular corticosteroids with placebo Absolute results not reported	RR 1.8 95% CI 1.3 to 2.3	●○○	corticosteroids
[8] Systematic review	Number of children not reported Data from 1 RCT Subgroup analysis	**Complete resolution of pain , 24 or 48 hours** with corticosteroids with placebo Absolute results not reported	Reported as not significant P value not reported The analysis is likely to have been underpowered to detect a clinically important difference between groups	⟷	Not significant
[8] Systematic review	Number of adults and children not reported 3 RCTs in this analysis Subgroup analysis	**Complete resolution of pain , 24 hours** with oral corticosteroids with placebo Absolute results not reported	RR 2.6 95% CI 1.6 to 4.3	●●○	corticosteroids
[8] Systematic review	Number of adults and children not reported 3 RCTs in this analysis Subgroup analysis	**Complete resolution of pain , 48 hours** with oral corticosteroids with placebo Absolute results not reported	RR 1.6 95% CI 1.2 to 2.1	●○○	corticosteroids
[8] Systematic review	Number of adults and children not reported 6 RCTs in this analysis	**Mean time to onset of pain relief** with oral or intramuscular corticosteroids with placebo Absolute results not reported	Mean difference 6.3 hours 95% CI 3.4 hours to 9.3 hours	○○○	corticosteroids
[8] Systematic review	Number of children not reported Subgroup analysis	**Mean time to onset of pain relief** with oral or intramuscular corticosteroids with placebo Absolute results not reported	Reported as not significant P value not reported	⟷	Not significant
[8] Systematic review	Number of adults and children with exudative sore throat not reported	**Mean time to onset of pain relief** with corticosteroids with placebo Absolute results not reported	Reported as not significant P value not reported Meta-analysis of RCTs where <50% of people had exudative sore throat	⟷	Not significant
[8] Systematic review	Number of adults and children testing as negative for bacterial pathogens not reported Subgroup analysis	**Mean time to onset of pain relief** with corticosteroids with placebo Absolute results not reported	Reported as not significant P value not reported	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[8] Systematic review	Number of adults and children not reported 5 RCTs in this analysis	**Mean time to complete resolution of symptoms (hours)** 15 to 45 hours with corticosteroids 35 to 54 hours with placebo	P value not reported The results were not pooled because of significant heterogeneity among trials in the direction of effect		

Recurrence

Compared with placebo We don't know whether corticosteroids are more effective at reducing recurrence (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Recurrence					
[8] Systematic review	Number of adults and children not reported 5 RCTs in this analysis	**Recurrent symptoms** with corticosteroids with placebo Absolute results not reported	4 RCTs reported no significant difference in recurrent symptoms, whereas one trial reported significantly increased recurrence in people receiving placebo Reported as significant/non-significant for each trial; no further data reported by review P value not reported	○○○	

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[8] Systematic review	125 people Data from 1 RCT	**Peritonsillar abcess** 1 person with corticosteroids 2 people with placebo Absolute results not reported	P value not reported		

Further information on studies

[8] Three RCTs identified by the review found no significant difference between corticosteroids compared with placebo in days missed from school or work (reported as not significant, P value not reported).

Comment: **Clinical guide:**
A single dose of corticosteroid seems to reduce pain earlier than placebo in adults, with or without evidence of streptococcal infection. We found no evidence of benefit for children.

OPTION PROBIOTICS TO REDUCE SYMPTOMS OF ACUTE INFECTIVE SORE THROAT

- For GRADE evaluation of interventions for Sore throat, see table, p 15 .
- Super-colonisation with *Streptococcus* isolated from healthy individuals apparently resistant to infections from

Streptococcus may reduce recurrence of sore throat, although there is currently no evidence to suggest it may treat symptoms of acute sore throat.

- We found no direct information about other probiotics, or about the effects of probiotics on the symptoms of acute sore throat.

Benefits and harms

Probiotics versus placebo:

We found one systematic review [6] (search date 1999, 2 RCTs [9] [10]) and one subsequent RCT [11] comparing super-colonisation with *Streptococcus* grown from a child resistant to infections from *Streptococcus* versus placebo (see comment below). We found no RCTs of other probiotics.

Recurrence

Compared with placebo Super-colonisation with Streptococcus seems effective at reducing recurrent sore throats at 2 to 3 months compared with placebo (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Recurrence					
[9] Systematic review	36 people aged 5 to 40 years with culture-confirmed recurrence of sore throat, all taking antibiotics In review [6]	**Recurrence of streptococcal sore throat , 3 months** 1/17 (6%) with super-colonisation with *Streptococcus* 11/19 (59%) with placebo	P <0.001	○○○	super-colonisation with *Streptococcus*
[10] Systematic review	130 people aged 3 to 59 years with culture-confirmed recurrence of sore throat, all taking antibiotics In review [6]	**Recurrence of streptococcal sore throat , 8 weeks** 22% with super-colonisation with *Streptococcus* 38% with placebo Absolute numbers not reported	P = 0.06	⟷	Not significant
[11] RCT	342 people, all treated with antibiotics	**Sore throat recurrence , mean 3 months** 36/189 (19%) with super-colonisation with *Streptococcus* 28/93 (30%) with placebo	P = 0.04	○○○	super-colonisation with *Streptococcus*

Symptom severity

No data from the following reference on this outcome. [6] [11]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[11] RCT	342 people, all treated with antibiotics	**Adverse effects** 36% with super-colonisation with *Streptococcus* 33% with placebo Absolute numbers not reported	Reported as equally tolerated P value not reported The authors suggested that the high rates of apparent adverse effects found in both groups were likely to be associated with the condition being treated	⟷	Not significant

No data from the following reference on this outcome. [6]

Further information on studies

Comment: Super-colonisation with *Streptococcus* isolated from healthy individuals apparently resistant to infections from *Streptococcus* is available only experimentally.

Clinical guide:
Probiotics may yet prove useful to reduce recurrence; there is no suggestion that they will improve acute symptoms of acute sore throat.

QUESTION What are the effects of interventions to prevent complications of acute infective sore throat?

OPTION ANTIBIOTICS TO PREVENT COMPLICATIONS OF ACUTE INFECTIVE SORE THROAT

- For GRADE evaluation of interventions for Sore throat, see table, p 15 .
- Antibiotics may reduce suppurative and non-suppurative complications of group A beta-haemolytic streptococcal pharyngitis, although non-suppurative complications are rare in industrialised countries.
- Antibiotics increase the risk of adverse effects, including gastrointestinal upset, rash, and vaginitis. Widespread antibiotic use may lead to bacterial resistance to antibiotics.

Benefits and harms

Antibiotics versus placebo:

We found one systematic review (search date 2008, 27 randomised or quasi-randomised trials, 12,835 people with sore throat, severity unclear) comparing antibiotics versus placebo to prevent complications of sore throat infection. [5]

Prevention of complications

Compared with placebo Antibiotics are more effective than placebo at reducing suppurative and non-suppurative complications of group A beta-haemolytic streptococcal pharyngitis (high-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Acute otitis media					
[5] Systematic review	3760 people 11 RCTs in this analysis	**Acute otitis media , 14 days** 11/2325 (0.5%) with antibiotics 28/1435 (2.0%) with placebo	RR 0.30 95% CI 0.15 to 0.58	●○○	antibiotics
Acute sinusitis					
[5] Systematic review	2387 people 8 RCTs in this analysis	**Acute sinusitis , 14 days** 4/1545 (0.3%) with antibiotics 4/842 (0.5%) with placebo	RR 0.48 95% CI 0.08 to 2.76	⟷	Not significant
Peritonsillar abscess (quinsy)					
[5] Systematic review	2433 people 8 RCTs in this analysis	**Peritonsillar abscess , 2 months** 2/1438 (0.1%) with antibiotics 23/995 (2.3%) with placebo	RR 0.15 95% CI 0.05 to 0.47	●○○	antibiotics

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Acute rheumatic fever and acute glomerulonephritis					
[5] Systematic review	10,101 people 16 RCTs in this analysis	**Acute rheumatic fever , 2 months** 37/5656 (0.7%) with antibiotics 74/4445 (1.7%) with placebo	RR 0.27 95% CI 0.12 to 0.60 The incidence of acute rheumatic fever has declined with time. The 111 cases of acute rheumatic fever assessed by the review all occurred in 10 trials undertaken between 1950 and 1961; there were no cases in the remaining 5 trials undertaken between 1987 and 2000	●○○	antibiotics
[5] Systematic review	5147 people 10 RCTs in this analysis	**Acute glomerulonephritis** 0/2927 (0%) with antibiotics 2/2220 (0.1%) with placebo	RR 0.22 95% CI 0.02 to 2.08	⟷	Not significant

Adverse effects

No data from the following reference on this outcome. [5]

Further information on studies

[5] The systematic review gave no information on adverse effects associated with the use of antibiotics. However, data from systematic reviews in people with other disorders suggested that antibiotics were associated with nausea, vomiting, headache, skin rash, and vaginitis (see reviews on acute bronchitis and acute otitis media in children).

[5] The review also assessed the effects of antibiotics on acute symptoms (see antibiotics to reduce symptoms of acute infective sore throat, p 5).

Comment: Acute rheumatic fever and acute glomerulonephritis associated with sore throat infection may be related to host antibodies to *Streptococcus* cross-reacting with host tissue in the heart and kidney. See also comment on antibiotics under treatments for sore throat, p 5 . In some populations, rheumatic fever may follow streptococcal skin infections or even non-streptococcal infections. [12] Best practice may be to advise use of antibiotics to treat sore throats only for those individuals or populations known to be at high absolute risk of rheumatic fever — for example, some Maori children in New Zealand. Widespread antibiotic use may lead to bacterial resistance to antibiotics (see review on acute bronchitis).

Clinical guide:
It seems reasonable to treat suppurative complications only if they arise. Antibiotics seem justified to prevent non-suppurative complications only in communities where the prevalence of non-suppurative complications remains high.

GLOSSARY

High-quality evidence Further research is very unlikely to change our confidence in the estimate of effect.

Low-quality evidence Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Moderate-quality evidence Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

SUBSTANTIVE CHANGES

Antibiotics to prevent complications of acute infective sore throat One previously included systematic review updated; [5] benefits and harms data enhanced, categorisation unchanged (Trade-off between benefits and harms).

Antibiotics to reduce symptoms of acute infective sore throat One previously included systematic review updated; [5] benefits and harms data enhanced, categorisation unchanged (Trade-off between benefits and harms).

Corticosteroids to reduce symptoms of acute infective sore throat One new systematic review added [8] suggesting that, in people taking antibiotics, corticosteroids reduce symptoms. Categorisation changed from Trade-off between benefits and harms to Likely to be beneficial in adults who are also taking antibiotics. Effects in children are uncertain.

NSAIDs Evidence reassessed. Categorisation changed from Likely to be beneficial to Trade-off between benefits and harms as even short-term use of NSAIDs may be associated with gastrointestinal and renal adverse effects.

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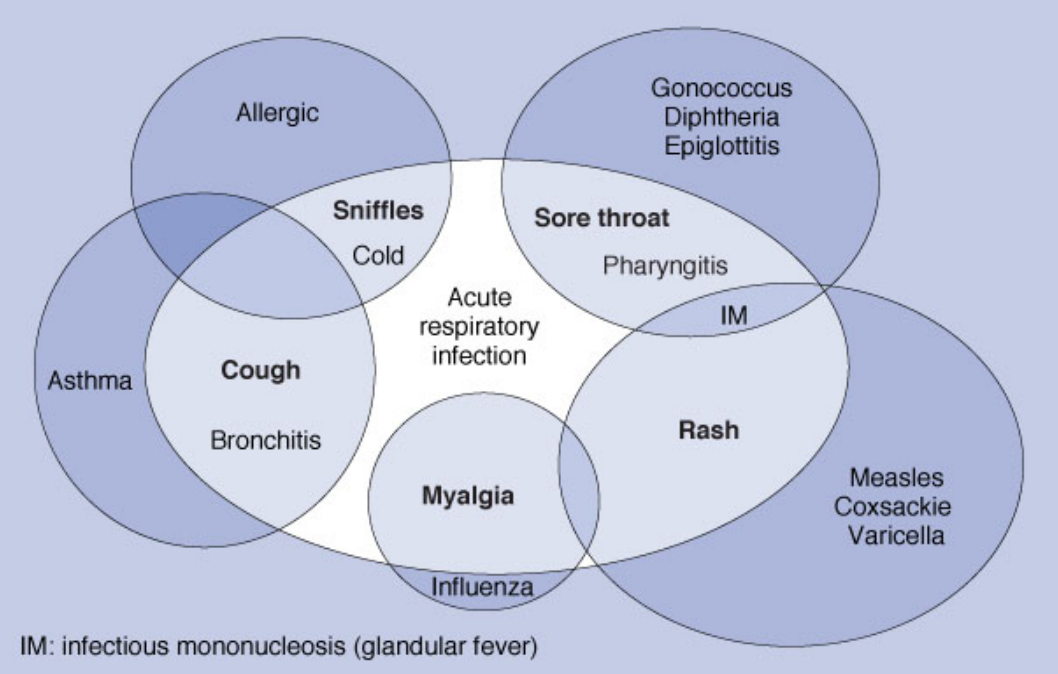

FIGURE 1 **Confusion and overlap in the classification of acute respiratory infections.**

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GRADE **Evaluation of interventions for Sore throat.**

Important outcomes	Prevention of complications, Recurrence, Symptom severity								
Studies (Participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
What are the effects of interventions to reduce symptoms of acute infective sore throat?									
4 (553) [6] [7]	Symptom severity	Analgesics versus placebo	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
12 (1189) [6]	Symptom severity	NSAIDs versus placebo	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
27 (12,835) [5]	Symptom severity	Antibiotics versus placebo	4	0	0	–1	0	Moderate	Directness point deducted for narrow inclusion criteria
4 (734) [8]	Symptom severity	Corticosteroids versus placebo in people receiving antibiotics	4	0	–1	0	0	Moderate	Consistency point deducted for different results in different subgroups
5 (unclear) [8]	Recurrence	Corticosteroids versus placebo in people receiving antibiotics	4	–1	–1	0	0	Low	Quality point deducted for incomplete reporting of results. Consistency point deducted for conflicting results
3 (448) [6] [11]	Recurrence	Probiotics versus placebo	4	0	–1	0	0	Moderate	
What are the effects of interventions to prevent complications of acute infective sore throat?									
16 (10,101) [5]	Prevention of complications	Antibiotics versus placebo	4	0	0	0	+1	High	Effect size point added for RR <0.5

We initially allocate 4 points to evidence from RCTs, and 2 points to evidence from observational studies. To attain the final GRADE score for a given comparison, points are deducted or added from this initial score based on preset criteria relating to the categories of quality, directness, consistency, and effect size. Quality: based on issues affecting methodological rigour (e.g., incomplete reporting of results, quasi-randomisation, sparse data [<200 people in the analysis]). Consistency: based on similarity of results across studies. Directness: based on generalisability of population or outcomes. Effect size: based on magnitude of effect as measured by statistics such as relative risk, odds ratio, or hazard ratio.